REMARKS

Claims 5, 6, 9, 11-18 and 20-29 and are currently pending in the present application. No new matter has been added by way of the present submission. For instance, claims 5 and 6 have been amended to more specifically define the structure and covalent attachment of the optional tag sequence as supported by the present specification as well as claim 12. Claim 9 has been amended to remove reference to the function of the polypeptide as well as to define additional structure as supported by the present specification at page 11, lines 16-21. Claims 11-17, and 20-24 have been amended to parallel amendments made to claim 9 and thus retain proper antecedent support. New claims 25 and 26 find support in claims 13 and 14, respectively, and new claims 27 and 28 find support in claims 23 and 24, respectively. Lastly, new claim 29 provides additional structure to the polypeptide of claim 9 as supported by the present specification at page 11, lines 22-25. Thus, no new matter has been added.

In view of the following remarks, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

Interview conducted on April 5, 2009

Applicants take this opportunity to thank the Examiner for the courtesies extended during the personal interview conducted on April 5, 2009. Applicants find that the Interview Summary dated April 12, 2009 substantially reflects the substance of the interview.

Issues Under 35 U.S.C § 112, First Paragraph, Written Description

1. Claims 5, 6, 17 and 18

Claims 5, 6, 17 and 18 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly

introducing "new matter" which does not have support within the specification. Applicants respectfully traverse this rejection.

Although the Examiner acknowledges that the present specification teaches a tag sequence attached covalently to the N- and/or C-termini of either amino acid 1587-1668 or amino acid 1596-1668 of SEQ ID NO: 1, the Examiner asserts that the specification fails to provide support for *non-covalently* attached tags. In an effort to further prosecution Applicants have amended claims 5 and 6 to recite "and an optionally included covalently attached tag sequence...."

Accordingly, Applicants submit that the rejection with respect to claims 5 and 6, as well as claims 17 and 18 that are dependent thereon, is moot. The Examiner is thus respectfully requested to withdraw this rejection.

2. Claims 9, 11-14, 17 and 20-24

Claims 9, 11-14, 17 and 20-24 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

The Examiner asserts that the claims contain subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor was in possession of the claimed invention at the time the application was filed. That is, the Examiner continues to assert that the claims encompass any amino acid sequence having 90% identity to amino acids 1587-1668 or amino acids 1596-1668 of SEQ ID NO: 1. The Examiner further asserts that the prior art and the specification do not describe a sufficient number of species that would represent the correlation between the structure of polypeptide and their

function as a substrate for ADAMTS-13 protease which cleaves between 1605-1606 of SEQ ID NO: 1. The Examiner indicates that the present specification lacks sufficient representative species within the variants encompassed by the claims. Because of this, the Examiner concludes that the specification and the prior art cannot describe the structure of the very broad claimed genus so that a skilled artisan would understand Applicants to have been in possession of the full scope of the claimed genus at the time of filing.

Applicants respectfully disagree with the Examiner.

Applicants have amended claim 9 as discussed during the personal interview conducted on April 5, 2009. Illustratively, claim 9 has been amended so as to remove all reference to the function of the polypeptide itself. This is consistent with similar language present in the Examples of the most recent U.S.P.T.O. Written Description Guidelines. Further, claim 9 has been amended to require the additional structure of a cleavage site between the 1605th and 1606th residues of SEQ ID NO:1 for ADAMTS-13.

Applicants stress that the 90% or higher sequence identity of claim 9 requires that at least 90% of the amino acids in the polypeptide will match those of the residues between 1587 and 1668 or 1596 and 1668 of SEQ ID NO:1, and up to 10% of them may vary. The specific disclosure of these particular stretches of amino acids, combined with the pre-existing knowledge in the art regarding the genetic code, its redundancies, and possible amino acids would have put one of ordinary skill in the art in possession of the genus of polypeptides having at least 90% sequence identity. With the use of a computer, one of skill in the art could have easily identified all of the possible polypeptide sequences falling within this genus.

Thus, Applicants submit that the specification fully satisfies the written description requirement for claim 9. Further, the new limitation to claim 9 (cleavage site) provides for additional structure to be shared among this genus of polypeptides. In summary, Applicants submit that those of skill in the art would understand that Applicants were in possession of the subject matter of claim 9 at the time of filing the present application. As such, the written description rejection with respect to claim 9 is moot. Moreover, due to their dependency upon claim 9, the same rejection of claims 11-14, 17 and 20-24 is likewise moot. The Examiner is therefore respectfully requested to withdraw this rejection.

Issue Under 35 U.S.C § 112, First Paragraph, Enablement

Claims 9, 11-14, 17 and 20-24 stand rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the enablement requirement. Applicants traverse this rejection.

The Examiner indicates that specification does not reasonably provide enablement for any isolated mutant substrate polypeptide for ADAMTS-13 protease having at least 90% of the amino acids 1587-1668 or amino acids 1596-1668 of SEQ ID NO: 1 since the mutation includes any substitution, deletion, insertion and any variation within the claimed amino acid regions. The Examiner continues to maintain that the claims continues to encompasses a very broad mutant having 90% or more sequence identity to a substrate consisting of amino acids 1587-1668 or 1596-1668 of SEQ ID NO: 1. Additionally the Examiner maintains that the prior art and present specification do not disclose any direction or guidance on how to make and use any other substrate polypeptide for ADAMTS-13 protease other than a fusion product of amino acids 1587-1668 or amino acids 1596-1668 of SEQ ID NO: 1.

Applicants respectfully disagree with the Examiner.

Claim 9 (upon which claims 11-14, 17 and 20-24 depend) relates to a particular genus of isolated polypeptide. The polypeptide has a cleavage site between the 1605th Tyr and 1606th Met of SEQ ID NO:1 for ADAMTS-13, and has an amino acid sequence identity of at least 90% or higher to a) a polypeptide, which begins at amino acid 1587 and ends at amino acid 1668 of the amino acid sequence of SEQ ID NO:1, or b) a polypeptide, which begins at amino acid 1596 and ends at amino acid 1668 of the amino acid sequence of SEQ ID NO:1.

Applicants respectfully submit that those of skill in the art are certainly able to make each these polypeptides. Moreover, using the combined knowledge in the art and the guidance of the present specification, those of skill in the art are able to use the claimed invention without undue experimentation. The combined knowledge provides sufficient direction as to how to use the presently claimed polypeptides as a substrate for ADAMTS-13.

Applicants further note that the Examiner refers to possible unpredictability in the art, specifically citing to Wu et al., "Characterization of a Core Binding Site for ADAMTS-13 in the A2 Domain of Von Willebrand Factor," PNAS, vol.103, no.49 p.18470-18474 (2006) (hereinafter "Wu"). The Examiner points to Wu as disclosing "It was unusual that an extended peptide sequence consisting of 10 before and 63 amino acids after the scissile bond, is necessary for recognition and cleavages by ADAMTS-13" (see Wu, top right column, page 18470). The Examiner thus concludes that the specification and prior art fail to sufficiently describe how to make and use the full scope of claimed genus.

Applicants submit that the Examiner has misinterpreted the significance of the disclosure of Wu. In fact, the above citation from Wu is simply a phrase to catch the attention of the reader. Indeed, Wu fully appreciates the significance of an extended sequence, which is exactly the point

of the present invention. Wu, which was published on December 5, 2005 and is therefore decidedly not prior art, is actually recognizing the significance of the present invention. However, the Examiner appears to believe that Wu's statement supports a finding of unpredictability. This misses the issue. That is, the issue is not one of whether an skilled artisan would find the invention unpredictable "before" the invention, but rather "after" the invention. To find otherwise would deprive the skilled artisan of the teachings of the present invention.

In fact, one of ordinary skill in the art brings to bear both their own knowledge and the knowledge imparted by the present invention, when making and using the present invention. Wu recognizes this point when it is stated that "The requirement of an extended substrate sequence and evidence of interaction along its length with ADAMTS-13 suggests that ... "(see Wu, bottom left column, page 18473). It is therefore apparent that Wu simply finds the extended peptide sequence to be unusual at first glance, but clearly recognizes that it is very important for recognition and cleavage by ADAMTS-13. Such sequences have been verified by the resent inventors as disclosed in the present specification, including the working examples and Figure 1.

Further, although the Examiner has already considered this fact (see pages 11-13 of the Reply filed on August 11, 2008), Applicants point out there has already been commercialization of FRETS-VWF73, regardless of the teachings of Wu.

To summarize, Applicants stress that Wu is not stating that the presently claimed subject matter is unpredictable. Wu is simply stating that the presently claimed subject matter was unexpected. This is significant in at least two regards. First, it shows that those of skill in the art fully appreciate the significance of the invention and are able to make and use the same without undue experimentation. This by itself defeats the Examiner's enablement rejection. And second,

the statements by Wu actually demonstrate surprise by artisans in the relevant field. Such evidence surely strengthens the non-obviousness of the present invention.

In view of the above, Applicants respectfully request that the Examiner withdraw the present enablement rejection.

Issue Under 35 U.S.C. § 102(b)

Claims 5, 6, 9, 11-14, 17-18 and 20-24 stand rejected under 35 U.S.C. § 102(b) as anticipated by Garfinkel et al., U.S. Patent No. 5,849,536 (hereinafter "Garfinkel") as evidenced by Wu. Applicants respectfully traverse.

The Examiner asserts that Garfinkel teaches the vWF GPIb binding domain polypeptide having residues disclosed as SEQ ID NO: 2 which comprises a polypeptide 100% identical to the polypeptide residues 1587-1668 or 1596-1668 of SEQ ID NO: 1.

The Examiner asserts that Example 4 (see Garfinkel, column 19, lines 40-41) teaches isolation of the polypeptide encoded by pVWF-VCL by "improved methods a purer and more active polypeptide is produced." Garfinkel's purified protein from Example 4 (SEQ ID NO: 2) contains 2049 amino acids, which is much larger than the present invention. However, the Examiner's states that Garfinkel's amino acids outside the amino acid regions of SEQ ID NO: 1 from the present invention meet the limitation of having a tag sequence attached at the N- or C-termini. The Examiner makes this assertion since the Examiner interprets the type of tag sequences broadly based on claim 12, which describes the tag sequence as either a protein or peptide.

Applicants respectfully traverse this rejection and submit that the Examiner's interpretation of the present "optional" tag is unreasonable since there is no evidence that the

flanking residues of Garfinkel are even able to assume such function. Regardless, Applicants have amended at least claims 5 and 6 to require specific types of optional tags that are distinct from any flanking sequence of Garfinkel.

CONCLUSION

In view of the above, Applicants submit that the pending application is in condition for allowance. The Examiner is thus requested to withdraw all rejections and allow the currently pending claims.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Craig A. McRobbie, Reg. No. 42,874, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____

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